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EXAMINER
COUNTS, GARY W

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/972,882	Applicant(s) MENDEL-HARTVIG ET AL.	
	Examiner Gary W. Counts	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12-19,21,22,24,25 and 27-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12-19,21,22,24,25 and 27-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the claims

The amendment entered April 28, 2003 is acknowledged and has been entered.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-10, 12-18, 25-28, 37 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because there appears to be a correlation step missing for the detection of the analyte. It is unclear how the analyte can be detected without the use of a label.

Claim 1 is vague and indefinite because the preamble of the claim does not correlate with the body of the claim. The preamble recites a method of determining an analyte in a sample. The body of the claim recites determining the concentration of analyte in the sample. It is recommended to include the determination of the concentration in the preamble of the claim.

Claim 1, step (a) is vague and indefinite because in step (b) the ratio is known or predetermined therefore the amount of receptor must be known or predetermined. It is recommended to include the known or predetermined amount of receptor.

Claim 1 is vague and indefinite because it is unclear what fraction is being isolated on the solid phase. Is a fraction of the analyte/receptor complex or a fraction of the unreacted receptor isolated on the solid phase or is some other fraction isolated?

Claim 7, line 4 "minor fraction" is vague and indefinite. It is unclear what is considered to be a minor fraction. There is no definition provided for the phrase in the specification.

Claim 14 "the detection reagent" there is insufficient antecedent basis for this limitation. See also deficiency found in claim 15.

Claim 15 is vague and indefinite because it is unclear how the receptor comprises a first part that binds specifically to the analyte, and a second part that binds to the solid phase and also comprises a label.

Claim 25 "said second amount" there is insufficient antecedent basis for this limitation. See deficiency found in the claims depending from claim 25.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 3, 7, 10-14, 31 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Sommer et al (US 5,569,608).

Sommer et al disclose a method for determining the concentration of analyte in a test fluid (abstract). Sommer et al disclose contacting the test fluid (sample) with an

excess of anti-hsa:gold sol conjugate (receptor) (col 6, line 64-65). Sommer et al disclose that this receptor binds specifically to the analyte to form an analyte/receptor complex. Sommer et al disclose a solid phase, which captures (isolates) analyte/receptor on one section of the solid phase and also captures (isolates) unreacted receptor on another section of the solid phase, thus fractionating the receptor (col 6, lines 45-67). Sommer et al discloses that the conjugate (receptor) is in the amount of 10 mg/ml (col 5, line 17) and that the immobilized receptor, which captures the analyte/receptor complex, is in the amount of 5 mg/ml (col 6, lines 54-55). Sommer et al disclose detecting the amount of analyte/receptor complex and determining the concentration of analyte.

With respect to the ratio of the isolated fraction of receptor and receptor contacted with the sample. Since Sommer teaches the amount of gold sol conjugated with receptor is in the amount of 10 mg/ml and that the amount of immobilized receptor, which captures the analyte/receptor complex, is in the amount of 5 mg/dl. Sommer et al anticipates the instantly recited ratio.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 19, 22, 24, 25, 27, 28,33, and 34-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sommer et al (US 5,569,608) in view of Bayer et al (The

Avidin-Biotin System, Immunoassay, Chapter 11, pages 237-267, 1996), Maggio et al (Enzyme-Immunoassay, p. 186-187, 1987)and Boguslaski et al (US 5,420,016).

See above for teachings of Sommer et al.

Sommer et al differ from the instant invention in failing to teach the receptor comprises a first part that binds specifically to the analyte, and a second part that binds to the solid phase. Sommer et al also fails to teach the components packaged into a kit.

Bayer et al disclose avidin-biotin systems used in immunoassays. Bayer et al disclose that avidin is immobilized to a solid phase (page 237 and 255). Bayer et al disclose biotinylation of an antibody and introducing the biotinylated antibody into the system for interaction with the avidin (page 239) Bayer et al disclose several advantages of the avidin-biotin system. Bayer et al disclose that the avidin-biotin system greatly improves performance of the immunoassay and improves the characteristics of the capture system (p. 237) and that there is more control over the immobilization procedure, since the amount of immunochemically active antibody molecules applied to the solid phase can be more precisely regulated (p. 255).

Boguslaski et al disclose assembling various components into a test kit. By assembling these components into test kits, it makes it more convenient and facile for the test operator (col 7, lines 8-11).

Maggio et al disclose immunoassay performed with a solid phase. Maggio et al disclose that the solid phase can be in the form of particles of cellulose, polyacrylamide or agarose, or the solid-phase carrier can be preformed into discs, tubes, beads, or microplates (p. 186)

It would have been obvious to one of ordinary skill in the art to biotinylate the receptor of Sommer et al and incorporate avidin as taught by Bayer et al because Bayer et al shows that this avidin-biotin system greatly improves performance of the immunoassay and improves the characteristics of the capture system and that there is more control over the immobilization procedure, since the amount of immunochemically active antibody molecules applied to the solid phase can be more precisely regulated.

It also would have been obvious to one of ordinary skill in the art to assemble the various reagents and components as taught by Sommer et al and Bayer et al into kits such as taught by Boguslaski et al because Boguslaski shows that test kits make it more convenient and facile for the test operator.

Sommer et al, Bayer et al and Boguslaski et al disclose the claimed invention except for a solid phase well. It would have been obvious to one of ordinary skill in the art at the time the invention was made to replace the solid phase of Sommer with the microplate of Maggio et al since the examiner takes Official Notice of the equivalence of solid phases (p. 186) for their use in immuoassays and the selection of any of these known equivalents to replace the solid phase of the Sommer et al reference would be within the level or ordinary skill in the art.

With respect to the ratios between said isolated fraction of analyte-binding receptor and analyte-binding receptor contacted with the sample as recited in the instant claims, the optimum ratio can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Further, It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a

result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

7. Claims 2, 8, 9,16, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sommer et al (US 5,569,608) in view of Bayer et al (The Avidin-Biotin System, Immunoassay, Chapter 11, pages 237-267, 1996).

See above for teachings of Sommer et al.

Sommer et al differ from the instant invention in failing to teach the receptor comprises a first part that binds specifically to the analyte, and a second part that binds to the solid phase.

Bayer et al disclose avidin-biotin systems used in immunoassays. Bayer et al disclose that avidin is immobilized to a solid phase (page 237 and 255). Bayer et al disclose biotinylation of an antibody and introducing the biotinylated antibody into the system for interaction with the avidin (page 239) Bayer et al disclose several advantages of the avidin-biotin system. Bayer et al disclose that the avidin-biotin system greatly improves performance of the immunoassay and improves the characteristics of the capture system (p. 237) and that there is more control over the

immobilization procedure, since the amount of immunochemically active antibody molecules applied to the solid phase can be more precisely regulated (p. 255).

It would have been obvious to one of ordinary skill in the art to biotinylate the receptor of Sommer et al and incorporate avidin as taught by Bayer et al because Bayer et al shows that this avidin-biotin system greatly improves performance of the immunoassay and improves the characteristics of the capture system and that there is more control over the immobilization procedure, since the amount of immunochemically active antibody molecules applied to the solid phase can be more precisely regulated.

With respect to the ratios between said isolated fraction of analyte-binding receptor and analyte-binding receptor contacted with the sample and the concentration of analyte as recited in the instant claims, the optimum ratio and concentration of analyte can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Further, It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

8. Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sommer et al in view of Hossom et al (US.4,623,461).

See above for teachings of Sommer et al.

Sommer et al differ from the instant invention in failing to teach contacting the sample with a liquid phase containing the receptor prior to contacting with the solid phase.

Hossom et al disclose contacting the sample with a liquid phase containing the receptor prior to the solid phase. Hossom et al disclose that this technique provides for a longer incubation period that affords more complete reaction and binding of the reactants, thereby increasing the sensitivity of the assay (col 5, lines 1-24).

It would have been obvious to one of ordinary skill in the art to combine the sample and receptor as taught by Hossom et al into the method of Sommer et al because Hossom et al shows that this technique provides for a longer incubation period that affords more complete reaction and binding of the reactants, thereby increasing the sensitivity of the assay.

9. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sommer et al in view of Singer et al (US 5,573,909).

See above for teachings of Sommer et al.

Sommer et al differ from the instant invention in failing to teach the label is a fluorophore or chromophore.

Singer et al disclose fluorophore labels which have very high fluorescence efficiency, typically with no apparent loss of signal intensity through the intermolecular energy process (col 11) and the ability to mix multiple transfer dyes with an initial donor

dye and an ultimate acceptor dye to increase the effective Stokes shift of the microparticles and thus tailor the microparticles to meet specific applications.

It would have been obvious to one of ordinary skill in the art to substitute the labels of Singer et al for the label of Sommer et al because Sommer et al disclose that any physically detectable signal may be used in his method and further because Singer et al teaches that these labels provide for very high fluorescence efficiency typically with no apparent loss of signal intensity through the intermolecular energy process and the ability to mix multiple transfer dyes with an initial donor dye and an ultimate acceptor dye to increase the effective Stokes shift of the microparticles and thus tailor the microparticles to meet specific applications.

10. Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sommer et al in view of Guan et al (US 6,316,205).

See above for teachings of Sommer et al.

Sommer et al differ from the instant invention in failing to specifically teach the sample is serum or whole blood.

Guan et al disclose a sandwich immunoassay in which the sample is a whole blood sample. The use of such a sample provides for a versatile assay device (col 5, lines 13-29).

It would have been obvious to one of ordinary skill in the art to use a whole blood sample as taught by Guan et al into the method of Sommer et al because Guan et al shows that the use of such a sample provides for a versatile assay device.

Response to Arguments

Applicant's argument (filed April 28, 2003) that the rejection of claims under 35 U.S.C. 102 (b) are not anticipated by either EP 0105714 or US 6,184,042 are found persuasive and therefore the rejection has been withdrawn. However, the newly applied reference Sommer et al anticipated the instantly recited claims as rejected above.

Applicant's argument that the label is not required has been fully considered but is not found persuasive. Applicant argues that the specification on page 6, lines 18-24 indicate that the detection reagent is usually labeled, however, it is also indicated that this method is not required and that it would be readily appreciated by one skilled in the art that the detection step can be performed by any one of a number well-known methods. This is not found persuasive because the only examples that the Applicant has provided involve the use of a detectable label. The applicant does not disclose any known method for detection without a label. Therefore, it is unclear what well known method applicant is referring to. Because the specification does not disclose a method without a label or provide a working example without a label. It is unclear how the analyte can be detected without the use of a label.

Conclusion

11. No claims are allowed.

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

LaMotte, III (US 5,296,347) disclose the use of receptors in immunoassay and teach the optimization of the receptors.

Kuo et al (US 6,183,972) disclose a method for determining the concentration of analyte in a fluid test sample and ratioing the signal of capture regions. However, Kuo et al specifically teach that the receptor is not in excess of that which is necessary to form conjugates with all of the analyte which would be expected to be present in the test sample (col 4, lines 36-38).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703)308-4242 for regular communications and (703)3084242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gary Counts
Examiner
Art Unit 1641
May 29, 2003

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05/30/03